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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,097	08/23/2001	Michael Hershfield	1579-527	7948

7590 10/15/2002

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EXAMINER
PATTERSON, CHARLES L JR

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,097	HERSHFIELD ET AL.	
	Examiner	Art Unit	
	Charles L. Patterson, Jr.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/12/02, 5/28/02 and 8/5/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 6-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election with traverse of Group V in Paper No. 7 is acknowledged. The traversal is on the ground(s) that (1) the instant application is a 371 and therefore the principles of unity of invention apply, (2) Groups (I-VI) and (VII-XII) would require a search of the same class and subclass, (3) all six enzymes of claim 5 should be examined in accordance with MPEP § 803.04, (4) for a restriction to be proper the two inventions must be independent and distinct, (5) Groups (I-VI) and (VII-XII) are not independent because they are directed to enzymes and the nucleic acids that encode them and (6) there would not be a serious burden upon the examiner to examine all the groups.

This is not found persuasive because of the reasons that follow, labeling each response as above. (1) The examiner admits that the wrong form paragraph was used and he should have used the unity of invention form paragraph, but the reasons if that form paragraph were used are the same as was stated in the instant restriction, the only appreciable difference being that the class and subclass and the reasons form paragraphs are not required in the unity of invention form paragraph, and some wording is a little different. The examiner does not intend to issue a unity of invention requirement because the groupings and reasons would be the same. (2) That certain groups would require a search of the same class and subclass does not necessarily mean the groups should be combined. Other things such as a consideration 35 USC § 112 issues and a search of the non-patent literature enter into examining different groups. Furthermore, as stated in the previous action, the enzymes and nucleic acids are each structurally different. (3) MPEP § 803.04 states that "up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction." This section mentions nucleotide sequences, not proteins, and furthermore one sequence is

"up to ten". (4) In MPEP § 802.01 the meaning of "independent" and "distinct" is discussed, along with a discussion of the legislative history of these terms in patent law. It is concluded in MPEP § 803 that restriction is proper when the inventions "are either independent (MPEP § 806.04 - §806.04(i)) or distinct (MPEP § 806.05 - § 806.05(i)) (emphasis added). (5) The groups directed to enzymes and those directed to nucleic acids are distinct because they are directed to different chemical compounds and furthermore the enzymes selected for examination (SEQ ID NO:10) is not encoded by any of the sequences in claims 6-15. (6) It is maintained that it would be a serious burden upon the examiner to examine all of the groups for the reasons listed *supra*. The examiner will examine Group XIII along with Group V.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-2 and 5 limited to the enzyme of SEQ ID NO:10 and claims 16-17 will be examined. Claims 3, 4 and 6-15 and claims 1-2 and 5 not limited to SEQ ID NO:10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 5 and 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is confusing in that it recited SEQ ID NOs that were not elected for prosecution.

Claims 16-17 are indefinite and confusing in the recitation of "non-deleterious PEG attachment sites. For what are the PEG attachment sites "non-deleterious"? Are they less antigenic than wild type, more antigenic

than wild type, have 100% of the activity of wild type, have >50% of the activity of wild type, are they more useful for purifying the enzyme, are they more useful as molecular weight markers, etc.?

Claims 16 and 17 are also confusing and incorrect in the recitation of "PEG attachment sites to a uricase protein". Apparently the correct recitation should be "PEG attachment sites in a uricase protein". The sites to be increased are residues of the uricase protein, not in PEG.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5 and 16-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

To start with, apparently the utility desired for this invention is to introduce Lys residues into mammalian uricase molecules such that when reacted with monomethoxypolyethylene glycol (PEG) the uricase has significant activity remaining but a much longer half-life in the serum of animals. This could be used to treat gout. The instant claims do not contain any of these limitations as to activity or increased half-life that would give it utility and therefore this utility rejection is being done.

Furthermore, SEQ ID NO:10 does not appear to have any utility specifically stated. On page 6, line 25-32 it is disclosed that SEQ ID NO:10 is a

PKS amino truncated uricase. PKS uricase is defined on lines 22-24 as one having residues 1-288 of porcine uricase and 289-304 of baboon uricase. It is taught on page 11, lines 12-19 that initial attempts to introduce 2 Arg-to-Lys substitutions into a baboon protein and substitution of a Glu to Lys at position 208 "resulted in an expressed mutant baboon protein which had greatly reduced uricase catalytic activity...[and that it] was apparent from this experiment that the ability to maintain uricase enzyme activity after arginine to lysine mutation of the mammalian DNA sequence was not predictable". Therefore, it is not predictable exactly what results will be obtained from any given Lys-modified uricase or uricase chimeric proteins, and absent some specific teaching as to what the characteristics of SEQ ID NO:10 are such as activity, half-life and antigenicity, this chimeric protein has no specific utility.

Claims 1, 2, 5 and 16-17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Mura, et al. (U). The instant reference teaches a uricase (urate oxidase) that is modified to insert a lysine. See the abstract and the first full sentence on page 145. Since "available non-deleterious PEG attachment sites" in claims 16-17 are not defined (see 35 USC § 112 second paragraph rejection, *supra*), these claims are also rejected. It is maintained that the PEG attachment sites are increased since a lysine is added. Whether this change is "non-deleterious" or not is not known for sure, especially in light of the fact that the term is not defined, and so for the purposes of this rejection it is maintained that the change is "non-deleterious".

Claims 1 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chau, et al. (AA) or Davis, et al. (AB) in view of Hershfield, et al. (V). Chau, et al. and Davis, et al. each teach the advantages of using PEG modified uricase molecules. Hershfield, et al. teach that additional PEG attachment sites can be introduced into enzymes by replacing arginine with lysine residues. As noted *supra*, it is not clear from the claim language exactly what "non-deleterious PEG attachment sites" are and therefore it is maintained that one of ordinary skill in the art would use the knowledge of the two primary references that PEG modification is advantageous for uricase and the teaching of Hershfield, et al. that more PEG attachment sites can be added to an enzyme by replacing arginine residues with lysine, to so replace the arginine residues. It is maintained that the addition

would have been non-deleterious at least for antigenicity, if not for other uses, absent very convincing proof to the contrary.

A copy of Hershfield, et al. (V) is not being sent because it is listed in the instant specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
October 11, 2002